



FLWEMS Paramedic Medication Information For:

## **THEOPHYLLINE**

Theophylline  
(thee-**OFF**-ih-lin)

### **Pregnancy Category**

**C Immediate-release**

### **Capsules, Tablets**

Bronkodyl Elixophyllin Quibron-T Dividose Slo-Phyllin Theolair. **Liquid Products:** Accurbron Aquaphyllin Asmalix Elixomin Elixophyllin Lanophyllin Pulmophylline\* Quibron-T/SR\* Slo-Phyllin Theoclear-80 Theolair Theolixir\* Theostat-80 Theophylline Oral. **Timed-release Capsules:** Slo-Bid Gyrocaps Slo-Phyllin Gyrocaps Theo-24 Theobid Duracaps Theoclear L.A.-130 Theoclear L.A.-260 Theospan-SR Theovent. **Timed-release Tablets:** Apo-Theo LA\* Novo-Theophyl SR\* Quibron-T/SR Dividose Respid Sustaire Theochron Theochron-SR\* Theo-Dur Theolair\* Theolair-SR Theophylline Extended-Release Theophylline SR Theo-Sav Theo-SR\* Theo-X T-Phyl Uni-Dur Uniphyll. (**Rx**)

### **Classification**

Antiasthmatic, bronchodilator

### **Action/Kinetics**

Theophylline stimulates the CNS, directly relaxes the smooth muscles of the bronchi and pulmonary blood vessels (relieve bronchospasms), produces diuresis, inhibits uterine contractions, stimulates gastric acid secretion, and increases the rate and force of contraction of the heart. Directly relaxes the bronchiolar smooth muscle (relieves bronchospasm) and pulmonary blood vessels. Although the exact mechanism is not known, theophyllines may alter the calcium levels of smooth muscle, blocking adenosine receptors, inhibiting the effect of prostaglandins on smooth muscle, and inhibiting the release of slow-reacting substance of anaphylaxis and histamine. Well absorbed from uncoated plain tablets and PO liquids. Time to peak serum levels, oral solution: 1 hr; uncoated tablets: 2 hr; chewable tablets: 1-1.5 hr; enteric-coated tablets: 5 hr; extended-release capsules and tablets: 4-7 hr. Therapeutic plasma levels: 10-20 mcg/mL. t<sub>1/2</sub>: 3-15 hr in nonsmoking adults, 4-5 hr in adult heavy smokers, 1-9 hr in children, and 20-30 hr for premature neonates. An increased t<sub>1/2</sub> may be seen in individuals with CHF, alcoholism, liver dysfunction, or respiratory infections. Because of great variations in the rate of absorption (due to dosage form, food, dose level) as well as its extremely narrow therapeutic range, theophylline therapy is best monitored by determination of the serum levels. In healthy adults, about 60% is bound to plasma protein whereas in neonates 36% is bound to plasma protein. Eighty-five percent to 90% metabolized in the liver and various metabolites, including the active 3-methylxanthine. Theophylline is metabolized partially to caffeine in the neonate. The premature neonate excretes 50% unchanged theophylline and may accumulate the caffeine metabolite. Excretion is through the kidneys (about 10% unchanged in adults).

### **Uses**

Prophylaxis and treatment of bronchial asthma. Reversible bronchospasms associated with chronic bronchitis, emphysema, and COPD. Oral liquid: Neonatal apnea as a respiratory stimulant. Theophylline and dextrose injection: Respiratory stimulant in neonatal apnea and Cheyne-Stokes respiration.

### **Contraindications**

Hypersensitivity to any xanthine, peptic ulcer, seizure disorders (unless on medication), hypotension, CAD, angina pectoris.

### **Special Concerns**

Use during lactation may result in irritability, insomnia, and fretfulness in the infant. Use with caution in premature infants due to the possible accumulation of caffeine. Xanthines are not usually tolerated by small children because of excessive CNS stimulation. Geriatric clients may manifest an increased risk of toxicity. Use with caution in the presence of gastritis, alcoholism, acute cardiac diseases, hypoxemia, severe renal and hepatic disease, severe hypertension, severe myocardial damage, hyperthyroidism, glaucoma.

### **Side Effects**

Side effects are uncommon at serum theophylline levels less than 20 mcg/mL. At levels greater than 20 mcg/mL, 75% of individuals experience side effects including N&V, diarrhea, irritability, insomnia, and

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headache. At levels of 35 mcg/mL or greater, individuals may manifest *cardiac arrhythmias* hypotension, tachycardia, hyperglycemia, *seizures*, *brain damage*, or *death*. *GI*: N&V, diarrhea, anorexia, epigastric pain, hematemesis, dyspepsia, rectal irritation (following use of suppositories), rectal bleeding, gastroesophageal reflux during sleep or while recumbent (theophylline). *CNS*: Headache, insomnia, irritability, fever, dizziness, lightheadedness, vertigo, reflex hyperexcitability, *seizures* depression, speech abnormalities, alternating periods of mutism and hyperactivity, *brain damage*, *death*. *CV*: Hypotension, *life-threatening ventricular arrhythmias* palpitations, tachycardia, *peripheral vascular collapse* extrasystoles. *Renal*: Proteinuria, excretion of erythrocytes and renal tubular cells, dehydration due to diuresis, urinary retention (men with prostatic hypertrophy). *Other*: Tachypnea, *respiratory arrest* fever, flushing, hyperglycemia, antidiuretic hormone syndrome, leukocytosis, rash, alopecia.

### **Laboratory Test Alterations**

↑ Plasma free fatty acids, bilirubin, urinary catecholamines, ESR. Interference with uric acid tests and tests for furosemide and probenecid.

### **Overdose Management**

*Symptoms*: Agitation, headache, nervousness, insomnia, tachycardia, extrasystoles, anorexia, N&V, fasciculations, tachypnea, *tonic-clonic seizures*. **The** first signs of toxicity may be seizures or ventricular arrhythmias. Toxicity is usually associated with parenteral administration but can be observed after PO administration, especially in children. *Treatment*: Have ipecac syrup, gastric lavage equipment, and cathartics available to treat overdose if the client is conscious and not having seizures. Otherwise a mechanical ventilator, oxygen, diazepam, and IV fluids may be necessary for the treatment of overdose. For postseizure coma, maintain an airway and oxygenate the client. To remove the drug, perform only gastric lavage and give the cathartic and activated charcoal by a large-bore gastric lavage tube. Charcoal hemoperfusion may be necessary. Treat atrial arrhythmias with verapamil and treat ventricular arrhythmias with lidocaine or procainamide. Use IV fluids to treat acid-base imbalance, hypotension, and dehydration. Hypotension may also be treated with vasopressors. To treat hyperpyrexia, use a tepid water sponge bath or a hypothermic blanket. Treat apnea with artificial respiration. Monitor serum levels of theophylline until they fall below 20 mcg/mL as secondary rises of theophylline may occur, especially with sustained-release products.

### **Drug Interactions**

*Allopurinol* / ↑Theophylline levels *Aminogluthethimide* / ↓Theophylline levels *Barbiturates* / ↓Theophylline levels *Benzodiazepines* / Sedative effect may be antagonized by theophylline *Beta-adrenergic agonists* / Additive effects *Beta-adrenergic blocking agents* / ↑Theophylline levels *Calcium channel blocking drugs* / ↑Theophylline levels *Carbamazepine* / Either ↑or ↓theophylline levels *Charcoal* / ↓Theophylline levels R/T ↑metabolism *Cimetidine* / ↑Theophylline levels *Ciprofloxacin* / ↑Theophylline plasma; ↑possibility of side effects *Corticosteroids* / ↑Theophylline levels *Digitalis* / ↑Digitalis toxicity *Disulfiram* / ↑Theophylline levels *Ephedrine and other sympathomimetics* / ↑Theophylline levels *Erythromycin* / ↑Theophylline effect R/T ↓liver metabolism *Ethacrynic acid* / Either ↑or ↓theophylline levels *Furosemide* / Either ↑or ↓theophylline levels *Halothane* / ↑Risk of cardiac arrhythmias *Interferon* / ↑Theophylline levels *Isoniazid* / Either ↑or ↓theophylline levels *Ketamine* / Seizures of the extensor-type *Ketoconazole* / ↓Theophylline levels *Lithium* / ↓Lithium effect R/T ↑rate of excretion *Loop diuretics* / ↓Theophylline levels *Mexiletine* / ↑Theophylline levels *Muscle relaxants, nondepolarizing* / ↓Muscle relaxation *Oral contraceptives* / ↑Theophylline effect R/T ↓liver metabolism *Phenytoin* / ↓Theophylline levels *Propofol* / ↓Sedative effect of propofol *Quinolones* / ↑Theophylline levels *Reserpine* / ↑Risk of tachycardia *Rifampin* / ↓Theophylline levels *St. John's wort* / Possible ↓theophylline plasma levels R/T ↑metabolism *Sulfapyrazone* / ↓Theophylline levels *Sympathomimetics* / ↓Theophylline levels *Tetracyclines* / ↑Risk of theophylline toxicity *Thiabendazole* / ↑Theophylline levels *Thyroid hormones* / ↓Theophylline levels in hypothyroid clients *Tobacco smoking* / ↓Theophylline effect R/T ↑liver metabolism *Troleandomycin* / ↑Theophylline effect R/T ↓liver metabolism *Verapamil* / ↑Theophylline effect *Zafirlukast* / Possible ↑theophylline levels

### **Additional Drug Interactions**

Possible ↑ Serum theophylline levels when used with zafirlukast.

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**How Supplied**

*Capsule*: 100 mg, 200 mg; *Capsule, extended release*: 50 mg, 75 mg, 100 mg, 125 mg, 130 mg, 200 mg, 250 mg, 260 mg, 300 mg; *Elixir*: 80 mg/15 mL; *Solution*: 80 mg/15 mL; *Syrup*: 80 mg/15 mL, 150 mg/15 mL; *Tablet*: 100 mg, 125 mg, 200 mg, 250 mg, 300 mg; *Tablet, extended release*: 100 mg, 200 mg, 250 mg, 300 mg, 400 mg, 450 mg, 500 mg, 600 mg

**Dosage**

•Capsules, Elixir, Oral Solution, Syrup, Tablets *Bronchodilator, acute attacks, in clients not currently on theophylline therapy.*

Adults and children over 1 year of age, loading dose: 5 mg/kg. Maintenance, Adults, nonsmoking: 3 mg/kg q 8 hr; Older clients, those with cor pulmonale: 2 mg/kg q 8 hr. Clients with CHF: 1-2 mg/kg q 12 hr; Children, 9-16 years of age and young adult smokers: 3 mg/kg q 6 hr; Children, 1-9 years of age: 4 mg/kg q 6 hr. Infants, 6-52 weeks, initial maintenance dose: Calculate as follows:  $[(0.2 \times \text{age in weeks}) + 5] \times \text{kg} = 24 \text{ hr dose in mg}$ . For infants up to 26 weeks, divide into q 8 hr dosing; for infants 26-52 weeks, divide into q 6 hr dosing.

*Bronchodilator, acute attacks, in clients currently receiving theophylline.*

Adults and children up to 16 years of age: If possible, a serum theophylline level should be obtained first. Then, base loading dose on the premise that each 0.5 mg theophylline/kg lean body weight will result in a 0.5-1.6-mcg/mL increase in serum theophylline levels. If immediate therapy is needed and a serum level cannot be obtained, a single dose of the equivalent of 2.5 mg/kg of anhydrous theophylline in a rapidly absorbed form can be given.

*Chronic therapy, based on anhydrous theophylline.*

Adults and children, initial: 16 mg/kg/24 hr, up to a maximum of 400 mg/day in three to four divided doses at 6-8-hr intervals; then, dose can be increased in 25% increments at 2-3 day intervals up to a maximum, as follows: Adults and children over 16 years of age: 13 mg/kg, not to exceed 900 mg/day; 12-16 years: 18 mg/kg/day; 9-12 years: 20 mg/kg/day; 1-9 years: 24 mg/kg/day.

•Extended Release Capsules and Tablets *Bronchodilator, chronic therapy, based on equivalent of anhydrous theophylline.*

Adults, initial: 6-8 mg/kg up to a maximum of 400 mg/day in three to four divided doses at 6-8-hr intervals; then, dose may be increased, if needed and tolerated, by increments of 25% at 2-3 day intervals up to a maximum of 13 mg/kg/day or 900 mg/day, whichever is less, without measuring serum theophylline. Pediatric, over 12 years of age, initial: 4 mg/kg q 8-12 hr; then, dose may be increased by 2-3 mg/kg/day at 3-day intervals up to the following maximum doses (without measuring serum levels): 16 years and older: 13 mg/kg/day or 900 mg/day, whichever is less; 12-16 years: 18 mg/kg/day.

•Elixir, Oral Solution, Syrup *Neonatal apnea.*

Loading dose: Using the equivalent of anhydrous theophylline administered by NGT, 5 mg/kg; maintenance: 2 mg/kg/day in two to three divided doses given by NGT.

•IV *Bronchodilator, acute attacks.*

See above doses using PO products.

**END OF INFORMATION – NOTHING FOLLOWS**